

# Rising Prostate-Specific Antigen Level After Prostatectomy

Naveen Kella, MD, Kevin M. Slawin, MD

Scott Department of Urology, Baylor College of Medicine, Houston, TX

[*Rev Urol.* 2004;6(2):89-92]

© 2004 MedReviews, LLC

## CASE REPORT

A 57-year-old man was referred to his urologist after a routine serum prostate-specific antigen (PSA) test revealed a level of 9.4 ng/mL. The patient denied any significant lower urinary tract voiding symptoms. He was sexually potent and denied any family history of prostate cancer. Urine dip analysis showed no evidence of hematuria or urinary tract infection. Digital rectal examination revealed a 30-g prostate without induration or nodularity. Because of the elevated serum PSA level, the patient underwent transrectal, systematic sextant, ultrasound-guided prostate biopsies at an outside urologist's clinic. The biopsies were sent for pathologic analysis as site-specifically labeled samples. Of the 6 cores obtained, the right-sided cores at the mid-prostate and apical prostate revealed Gleason 8 (4 + 4) adenocarcinoma. The maximum length of cancer was 6 mm, or 50% of the apical core.

Following the biopsy results, computed tomography (CT) of the pelvis and a bone scan demonstrated no evidence of lymphadenopathy or bone metastasis. The patient discussed various options with his urologist, who referred him to us for further evaluation and treatment. After consultation with us, including review of the pathology, which confirmed the original findings, the patient opted for a radical retropubic prostatectomy and bilateral pelvic lymph node dissection. A repeat PSA measurement during his consultation 1 month after the biopsy revealed a level of 15.7 ng/mL, although the results were obtained from a different laboratory and manufacturer's assay. Tumor

Table 1  
Ultrasensitive Prostate-Specific Antigen (uPSA) Assay Results

Date	Postoperative Day	uPSA Level (ng/mL)
1/22/2003	42	0.034
3/13/2003	93	0.047
4/29/2003	140	0.057
6/10/2003	182	0.068

markers drawn per a research protocol showed interleukin-soluble receptor and transforming growth factor  $\beta$  levels of 38.3 ng/mL and 1.1 ng/mL, respectively.

An open, mini-incision, left, unilateral, nerve-sparing radical retropubic prostatectomy with contralateral neurovascular bundle resection and sural nerve grafting was performed without complications. Final pathology revealed a Gleason 8 (4 + 4) adenocarcinoma with focal extracapsular extension and negative surgical margins. Lymph nodes were negative (pT3aNOM0).

Postoperatively, the patient was monitored with an ultrasensitive PSA assay (uPSA) (Clinical Pathology Laboratories, Austin, Tex, using the Third-Generation Immulite PSA assay, DPC) beginning 6 weeks (42 days) after surgery and every 3 months thereafter. The results are shown in Table 1.

## MANAGEMENT OPTIONS

The next appropriate step is:

1. Continued observation until uPSA level is greater than 0.2 ng/mL
2. Repeated bone scan, CT scan, and/or indium 111-capromab pendetide immunoscintigraphy (ProstaScint scan)
3. Immediate or delayed androgen deprivation therapy
4. Salvage radiotherapy

Vote online at [www.medreviews.com](http://www.medreviews.com); fax your response to MedReviews at (212) 971-4047; or e-mail your selection to [dgern@medreviews.com](mailto:dgern@medreviews.com).

## Discussion of Last Issue's Case Scenario

### IN THE LAST ISSUE, DR ROEHRBORN PRESENTED THIS CASE REPORT:

A 39-year-old white man presents with a long history of lower urinary tract symptoms. He admits to both irritative and obstructive voiding symptoms, which have persisted most of his adult life. He denies any history of sexually transmitted disease, urinary tract infections, or trauma or surgery of the lower urinary tract.

The patient's self-administered International Prostate Symptom Score (IPSS) is 24 of a possible 35 points. He performs 2 voids, which demonstrate a maximum flow rate of 11.8 mL/s with a voided volume of 368 mL (Figure 1) and 9.8 mL/s with a voided volume of 195 mL. Residual urine as determined by ultrasound is 75 mL. Physical

examination is unremarkable, and digital rectal examination reveals a small prostate of approximately 25 g to 30 g. Urinalysis is essentially negative. Serum prostate-specific antigen level is measured and found to be 1.1 ng/mL.

A trial of tamsulosin, 0.4 mg daily, is initiated. After 4 weeks of treatment, the patient returns to the office and reports marginal improvement in his symptoms. A doubling of the dosage is suggested, and tamsulosin, 0.8 mg daily, is taken for an additional 4 weeks. Upon his return visit, the patient complains of absent ejaculation, which is disturbing to him. His symptoms have not improved further, and his IPSS is now 19 points (moderate to severe).

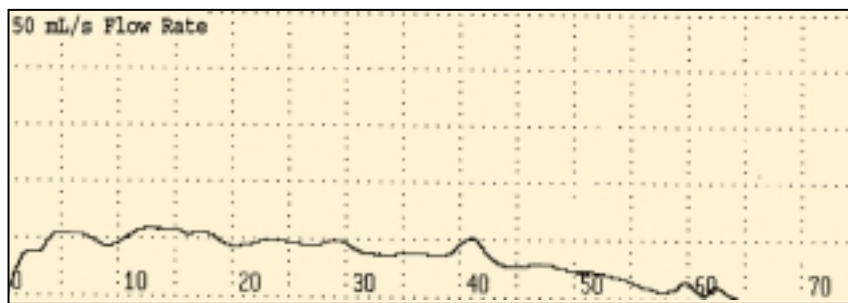


Figure 1. Typical free flow rate recording in a patient with bladder neck obstruction, demonstrating a maximum flow rate of 11.8 mL/s and a prolonged voiding time of 64 seconds.

### THE FOLLOWING QUESTIONS REGARDING PATIENT MANAGEMENT WERE ASKED:

Which statement regarding management of this patient is most accurate?

- ☐ 1. The patient is likely to experience additional symptom improvement by increasing the tamsulosin dosage to 1.2 mg daily.
- ☐ 2. The patient should be switched to another  $\alpha$ -blocker to achieve further symptom improvement.
- ☐ 3. A 5- $\alpha$ -reductase inhibitor should be added to the treatment regimen.
- ☐ 4. The absent or retrograde ejaculation is not a class effect of  $\alpha$ -blockers.
- ☐ 5. Absent ejaculation signals treatment efficacy in patients with lower urinary tract symptoms treated with tamsulosin.

The next most appropriate step in the management of this patient would be:

- ☐ 1. Flexible urethrocystoscopy in the office to rule out a urethral stricture
- ☐ 2. One-month treatment course with a quinolone antibiotic
- ☐ 3. Videourodynamics
- ☐ 4. Cystometrogram
- ☐ 5. Transurethral resection of the prostate

## AUTHOR'S DISCUSSION

This 39-year-old man's LUTS are not likely to be the result of benign prostatic hyperplasia (BPH), the prevalence of which begins to increase after the age of 40 years and reaches approximately 60% for men in their sixties.<sup>1</sup> The more likely explanation for this patient's symptoms is a urethral stricture or bladder neck obstruction. The urinary flow rate pattern (Figure 1) does not suggest a urethral stricture, which is characterized not only by a reduced maximum flow rate but also by a flat maintained peak flow rate indicative of the inability of the urethral diameter to stretch further with increasing detrusor pressure (Figure 2). The absence of any trauma, instrumentation, or sexually transmitted diseases also makes this diagnosis unlikely.

Treatment with an  $\alpha$ -blocker is appropriate therapy for young men with bladder neck obstruction.<sup>2</sup> This condition occurs frequently in young men and is often misdiagnosed as prostatitis. Following the National Institutes of Health nomenclature, the absence of bacterial infection would allow a classification of chronic pelvic pain syndrome (CPPS) type IIIA or IIIB (with or without inflammatory cells in the expressed prostatic secretions, respectively).<sup>3</sup> A primary bladder neck obstruction may or may not be associated with pelvic pain and/or sexual dysfunction, the combination of which is the hallmark of CPPS.

After failure to achieve satisfactory symptom relief, it is appropriate to increase the dosage of tamsulosin from 0.4 mg to 0.8 mg daily.<sup>4</sup> There is no evidence that increasing the tamsulosin dosage to 1.2 mg daily would further improve symptoms. Furthermore, the various  $\alpha$ -blockers have similar efficacy spectrums and, therefore, switching to a different  $\alpha$ -blocker is unlikely to further improve the patient's symptoms.

Although finasteride has been shown to have efficacy in men with CPPS type III,<sup>5</sup> men with bladder outlet obstruction are unlikely to benefit from the addition of a 5- $\alpha$ -reductase inhibitor. Among  $\alpha$ -blockers, tamsulosin has a unique adverse event profile. Up to 18% of patients

receiving tamsulosin, 0.8 mg daily, experience retrograde ejaculation or anejaculation.<sup>4</sup> However, retrograde ejaculation and anejaculation are not class effects of  $\alpha$ -blockers, and similar incidence rates are not reported with other agents. There is no evidence that the presence of retrograde ejaculation or anejaculation is a sign that the treatment is likely to be effective. This conclusion is tempting, as an effect of  $\alpha$ -blockers is to relax the bladder neck, which in turn may cause backflow of seminal fluid into the bladder during ejaculation. However, there is no correlation between the presence of these conditions and symptomatic or urodynamic improvement. Although the exact mechanism by which this ejaculatory disturbance occurs is not known, it may be related to tamsulosin's effect on the  $\alpha_{1D}$  receptor in the vas deferens and seminal vesicles.<sup>6</sup>

Flexible office urethrocystoscopy might help to rule out urethral stricture disease; however, this is not a likely diagnosis based on the patient's flow rate and history. Although prolonged treatment courses with quinolone antibiotics have been shown to have marginal efficacy in men with nonbacterial prostatitis or CPPS type III, they do not play a major role in the treatment of bladder outlet obstruction. Videourodynamics, but not a simple cystometrogram, would shed further light on the cause of this patient's symptoms. Whereas a cystometrogram would only allow for assessment of the response of the bladder to filling, videourodynamics would help to identify not only the presence of obstruction but also the exact anatomical location of the obstruction, which would be most helpful in the case of this patient who failed  $\alpha$ -blocker therapy. Given the unlikely scenario of true BPH being the cause of this patient's symptoms, transurethral resection of the prostate would be most inappropriate.

Bladder neck obstruction in young men is a vexing condition that is frequently encountered by physicians engaged in the management of men with LUTS. Because

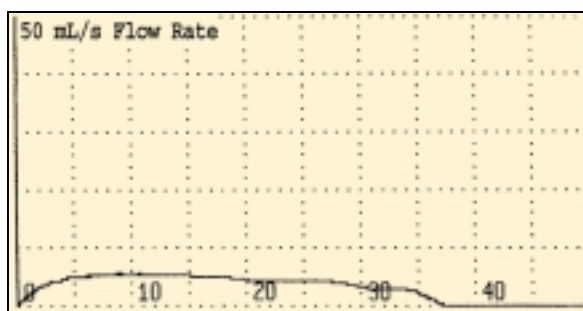


Figure 2. Typical flow rate recording in a patient with urethral stricture, demonstrating the fixed opening that is not further dilated by the flow and detrusor pressure during voiding as is commonly seen in patients with benign prostatic hyperplasia.

LUTS in general are nonspecific and nondiagnostic, other conditions to which these symptoms can be attributed need to be ruled out, including BPH, urethral stricture, various forms of prostatitis, and carcinoma in situ of the bladder. Given this patient's age, history, flow rate pattern, digital rectal examination, relatively low PSA level, normal urinalysis, and lack of other hallmarks of CPPS type IIIA or IIIB, the most likely diagnosis is bladder outlet obstruction. Initial treatment with an  $\alpha$ -blocker is appropriate, as is increasing the dosage from 0.4 mg/d to 0.8 mg/d, as suggested in the tamsulosin package insert, when sufficient symptom relief is not achieved. Surgical treatments, such as endoscopic incision or resection of the bladder neck, are highly effective but should be reserved for men with a urodynamically proven obstruction at the bladder neck who have failed  $\alpha$ -blocker therapy. The irreversible nature of retrograde ejaculation following bladder neck incisions dictates a judicious choice of

this form of treatment in young men potentially interested in future fertility. ■

#### References

1. Roehrborn C, McConnell J. Etiology, pathophysiology, epidemiology and natural history of benign prostatic hyperplasia. In: Walsh P, Retik A, Vaughan E, et al, eds. *Campbell's Urology*. 8th ed. Philadelphia: WB Saunders; 2002:1297-1336.
2. Nickel JC. The use of alpha1-adrenoceptor antagonists in lower urinary tract symptoms: beyond benign prostatic hyperplasia. *Urology*. 2003;62(3 suppl 1):34-41.
3. Krieger JN, Ross SO, Deutsch L, et al. The NIH Consensus concept of chronic prostatitis/chronic pelvic pain syndrome compared with traditional concepts of nonbacterial prostatitis and prostatodynia. *Curr Urol Rep*. 2002;3:301-306.
4. Narayan P, Evans CP, Moon T. Long-term safety and efficacy of tamsulosin for the treatment of lower urinary tract symptoms associated with benign prostatic hyperplasia. *J Urol*. 2003;170(2 pt 1):498-502.
5. Downey J, Nickel J, Pontari M, et al. Randomized placebo controlled multicenter pilot study to evaluate the safety and efficacy of finasteride in the treatment of male chronic pelvic pain syndrome: category IIIA CPPS [abstract]. *J Urol*. 2002;167(suppl):27A.
6. Andersson KE. Alpha-adrenoceptors and benign prostatic hyperplasia: basic principles for treatment with alpha-adrenoceptor antagonists. *World J Urol*. 2002;19:390-396.